American Journal of Hematology 57:87–88 (1998)

Successful Treatment of Acquired Factor VIII Inhibitors With Cyclosporin

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The treatment of Factor VIII inhibitors remains controversial and no standard therapy exists. We describe in this report two consecutive patients with this inhibitor that responded to cyclosporin. Clinical improvement of the bleeding diathesis, a return to normal of the PTT, a decrease in the level of the inhibitor, and a return to normal of the factor VIII level followed use of this drug. We believe that cyclosporin is effective in the treatment of factor VIII inhibitors and deserves further investigation. Am. J. Hematol. 57:87–88, 1998. © 1998 Wiley-Liss, Inc.

Key words: factor VIII; inhibitor; treatment; cyclosporin; coagulopathy

INTRODUCTION

Factor VIII inhibitors are most commonly associated with hemophilia, but other conditions such as pregnancy, neoplasia, and autoimmune disorders can lead to their formation [1,2]. The prompt treatment of these inhibitors is important because of associated severe bleeding and mortality. The traditional treatments consist of factor VIII replacement to raise the factor VIII level and concomitant immunosuppression [1,3–6]. We report on two patients with severe bleeding and the presence of factor VIII inhibitors that responded rapidly and effectively to the use of cyclosporin.

MATERIALS AND METHODS

Case 1

A 35-year-old pregnant female with a PTT of 68 sec was admitted for an elective cesarean section. Factor VIII deficiency was diagnosed and treatment was initiated with porcine factor VIII concentrate (Hyate C) with rapid correction of this PTT. Cesarean delivery was performed with an uneventful post-operative course. One month later, she was readmitted with an anterior compartment syndrome of the right leg. The PTT was 89 sec and the factor VIII level was .03 U/ml (Table I). Despite a loading dose and continued treatment with porcine factor VIII, the PTT remained unchanged and an emergency fasciotomy was performed. The patient developed thrombocytopenia, with no evidence of D.I.C. and a normal bone marrow aspirate, which was attributed to the porcine factor VIII [7,8]. Concurrent treatments included corticosteroids 2 mg/kg, gamma globulin 60 g/d, and amino caproic acid 1 g/2hr. Despite aggressive management, her hemoglobin decreased by 60 g/L. Cyclosporin 100 mg po bid was started following discontinuation of other immunosuppressives with rapid improvement in her clinical status (Table I).

Case 2

A 70-year-old female was admitted for confusion, dyspnea, and anemia with a hemoglobin of 51 g/L with normal indices. Gastroscopy revealed a large gastric ulcer that was not actively bleeding. The PTT on presentation was 86 sec. The patient was transfused and started on cyclosporin 100 mg bid without factor VIII replacement (Table I).

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Received for publication 31 July 1997; Accepted 27 August 1997

RESULTS

TABLE I. Results of Two Patients With Factor VIII Inhibitors Treated With Cyclosporin*

	Patient 1	Patient 2
Age in years	35	70
PTT on admission	89	86
PTT-start of CSP	97	87
PTT at day 5	69	61
PTT at day 10	56	46
PTT-prior to discharge	39	31
Factor VIII level on admission	0.03	0.06
Factor VIII level at start of Rx	0.03	0.06
Factor VIII level post Rx	0.52	0.91
BU-human	14.4	7.4
BU-porcine	7.2	0.0
CSP level-mean	213	233
Outcome	Off CSP, no inhibitor × 24 m	Off CSP, no inhibitor × 20 m

*PTT, activated partial thromboplastin time in seconds (normal 35–43 sec); Rx, treatment; BU, Bethesda unit; CSP, cyclosporin.

DISCUSSION

Factor VIII inhibitors occur in hemophilia and other conditions including pregnancy, malignancy, and autoimmune disorders [1,2]. The non-hemophiliac inhibitors in general are associated with severe bleeding and death is not uncommon [1,2,5]. Treatment consists of factor VIII replacement and concomitant immunosuppression [3–7], however treatment is unpredictable and no standard therapy exists [8].

We report on the successful use of cyclosporin in the treatment of two consecutive patients with factor VIII inhibitors. Both patients presented with a severe bleeding diathesis and a prolonged PTT. The first patient failed first line intervention with drugs recommended for this disorder, but improved with use of cyclosporin. The second patient received only cyclosporin and transfusions with no factor VIII replacement. Neither patient manifested problems of hypertension, electrolyte imbalance, or renal dysfunction. Both patients maintain normal coagulograms with no evidence of bleeding and are off cyclosporin. These remissions have been maintained for 24 and 20 months following presentation.

We are not the first to report cyclosporin use in this disorder. However, the previously reported patient was heavily pretreated with cyclophosphamide and was on concurrent corticosteroids in marked contrast to both patients in this report [9]. Although its mechanism of effect is unclear, preliminary data do not suggest that cyclosporin interferes with attachment of antibody to its epitope (data not shown). Because treatment of this disorder is often problematic and not always successful, further studies are necessary to determine the place of cyclosporin in the treatment of this disorder.

ACKNOWLEDGMENTS

The authors thank Sandoz Canada for supplying cyclosporin for these two patients. We also thank Sophia Vranas for her secretarial support and Dr. L. Moroz for suggestions and technical assistance.

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